## Association of human mtDNA mutations with autism in Iranian patients

Sir,

Autism spectrum disorders (ASD) are the most heritable complex disorders. [1,2] Although there have been many efforts to locate the genes associated with ASD risk, the genetics of ASD has not been elucidated. [3-5] Some studies have confirmed the contribution of mitochondrial genome mutations to the pathophysiology of autism, [4,6] but other studies have rejected such a contribution. [7] In the current study (research project number #17), we have investigated the association between mitochondrial tRNA gene mutations and the risk of autism.

Deoxyribonucleic acid (DNA) was extracted from the blood of 24 ASD patients in the Special Medical Center of Tehran, Iran, during 2010-2011, and 40 age-matched, healthy controls (QIAamp DNA Micro kit, Germany). Twenty-two tRNA genes of the mitochondrial genome were polymerase chain reaction (PCR)-amplified, using 12 primer pairs, and then sequenced. The sequencing results were screened for mutations using the clustalW Program and the association of the mutations with autism risk was assessed by statistical analysis, using the SPSS version 15.

Many of the observed mutations were sporadic mutations without any significant relationship with the risk of autism, while other mutations, including those of high frequency, showed no significant relationship with the risk of disease (*P*-value > 0.05), except mutations 16126T>C (*P*-value = 0.01), 14569G>A (*P*-value = 0.02), and 1811A>G (*P*-value = 0.04). These three mutations were in the non-coding regions of the mitochondrial genome, near the tRNA genes. The mutation 16126T>C was in the mtDNA control region.

Our study showed a significant relationship between the point mutations 16126T>C, 14569G>A, and 1811A>G of the mitochondrial genome and the risk of autism.

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## **REFERENCES**

- Bayou N, M'Rad R, Ahlem B, Bechir Helayem M, Chaabouni H. Autism: An overview of genetic aetiology. Tunis Med 2008;86:573-8.
- Muhle R, Trentacoste SV, Rapin I. The genetics of autism. Pediatrics 2004;113:e472-86.
- Rossignol DA, Frye RE. Mitochondrial dysfunction in autism spectrum disorders: A systematic review and meta-analysis. Mol Psychiatry 2011;17:290-314.
- Weissman JR, Kelley RI, Bauman ML, Cohen BH, Murray KF, Mitchell RL, et al. Mitochondrial disease in autism spectrum disorder patients: A cohort analysis. PLoS One 2008;3:e3815-20.
- Zhang B, Angelidou A, Alysandratos KD, Vasiadi M, Francis K, Asadi S, et al. Mitochondrial DNA and anti-mitochondrial antibodies in serum of autistic children. J Neuroinflammation 2010;7:80-4.
- Virgilio R, Ronchi D, Bordoni A, Fassone E, Bonato S, Donadoni C, et al. Mitochondrial DNA G8363A mutation in the tRNA Lys gene: Clinical, biochemical and pathological study. J Neurol Sci 2009;281:85-92.
- Alvarez-Iglesias V, Mosquera-Miguel A, Cusco I, Carracedo A, Perez-Jurado LA, Salas A. Reassessing the role of mitochondrial DNA mutations in autism spectrum disorder. BMC Med Genet 2011;12:50-6.